

## REMARKS

New Tables 4 and 5 are provided to substitute for original Tables 4 and 5 found at pages 68-76. The Substitute Tables 4 and 5 provide reference to the SEQ ID Nos. found in the Sequence Listing. A set of marked-up Tables 4 and 5 is also provided with highlighting to show the changes from the original Tables 4 and 5. No new matter has been entered.

A Sequence Listing paper copy is also provided for insertion into the Specification.

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It is believed that no additional fee is due; however, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Deposit Account No. 01-2508/11362.0038.NPUS01.

The Examiner is invited to contact the undersigned attorney at (713) 787-1438 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: October 27, 2003

**Table 4.** Differential expression of Apo E isoforms in AD patients versus contrast groups.

Apo E NPI	pI	MW (kDa)	6 AD vs. 6 D	6 AD vs. 6 FTD	6 AD vs. 10 FTD	6 AD vs. 4 VAD	Aa # start-end	Peptide sequence #	Seq ID No.
34	5.11	35.2	↓	=	=	=	270-278	LQAEAFQAR	1
							259-269	AKLEEQAQQIR	2
							166-175	LLRDADDLQK	3
							19-33	KVEQAVETEPEPELR	4
35	5.32	34.3	↓	nd	nd	nd	270-278	LQAEAFQAR	1
							259-269	AKLEEQAQQIR	2
							199-207	LGPLVEQGR	5
							301-317 (C-term.)	VQAAVGTSAAPVPSDNH	6
72	5.07	15.8	=	=	nd	nd	199-207	LGPLVEQGR	5
							270-278	LQAEAFQAR	1
							259-269	AKLEEQAQQIR	2
73	5.11	15.8	=	=	=	=	270-278	LQAEAFQAR	1
74	4.91	15.8	=	=	=	↓	199-207	LGPLVEQGR	5
							270-278	LQAEAFQAR	1
							259-269	AKLEEQAQQIR	2
							210-224	AATVGSAGQPLQER	7
							138-152	GEVQAMLGQSTEELR	8
							94-108	SELEEQLTPVAEETR	9
							301-317 (C-term.)	VQAAVGTSAAPVPSDNH	6
75	5.09	15.1	=	nd	nd	nd	138-152	GEVQAMLGQSTEELR	8
							19-33	KVEQAVETEPEPELR	4
							270-278	LQAEAFQAR	1
41	5.07	15.3	↓	nd	nd	nd	19-33	KVEQAVETEPEPELR	4
							270-278	LQAEAFQAR	1
76	5.24	13.8	=(↓)	↓	=	↓	210-224	AATVGSAGQPLQER	7
77	4.96	12.4	=(↑)	=	=	=	259-269	AKLEEQAQQIR	2
52	5.30	33.8	↓	nd	nd	nd	270-278	LQAEAFQAR	1

**Table 4.** Differential expression of Apo E isoforms in AD patients versus contrast groups.

Apo E NPI	pI	MW (kDa)	6 AD vs. 6 D	6 AD vs. 6 FTD	6 AD vs. 10 FTD	6 AD vs. 4 VAD	Aa # start-end	Peptide sequence #	Seq ID No.
							199-207	LGPLVEQGR	5
							259-269	AKLEEQAQQIR	2
							80-90	ALMDETMKELK	10
60	5.38	15.6	↓	nd	nd	nd	19-33	KVEQAVETEPEPELR	4
66	5.17	30.	↑QL	nd	nd	nd	199-207	LGPLVEQGR	5
							91-109	AYKSELEEQLTPVAEETR	11
							111-121	LSKELQAAQAR	12
							210-224	AATVGSAGQPLQER	7
							259-269	AKLEEQAQQIR	2
							270-278	LQAEAFQAR	1
11	5.22	35.3	nd	↓QL	nd	nd	19-33	KVEQAVETEPEPELR	4
							91-109	AYKSELEEQLTPVAEETR	11
							111-121	LSKELQAAQAR	12
							210-224	AATVGSAGQPLQER	7
							259-269	AKLEEQAQQIR	2
							270-278	LQAEAFQAR	1

Only quantitative results are showed (with the exception of NPI 66 and NPI 11, where only a qualitative difference (QL) was found).

↓: down-regulated in AD {↓:  $p < 0.05$ ; = (↓):  $p < 0.07$ }

↑: upregulated in AD {↑:  $p < 0.05$ ; = (↑):  $p < 0.07$ }

=: no significant difference

#: peptide sequences covered by MS analysis

nd: not detected

**Table 5.** Identification of the protein spots that were altered between the studied groups.

Spot exp1	Spot exp2	Peptide	Seq ID No.	aa	Identification in database	ID number database
2713	674	TDTSHHDQDHPFNK	13	35-49	Alpha-1-antitrypsin	P01009
		LVDFKFLQ	14	150-159		
		FLEDFK	15	154-160		
		KQINDYVEK	16	179-187		
		QINDYVEK	17	180-187		
		DTEEDFHVDQATTVK (M1A allele)	18	226-241		
		DTEEDFHVDQVTTVK (M1V allele)	19	226-241		
		LQHLENELTHDIITK	20	284-298		
		FLENEDR	21	299-305		
		FLENEDRR	22	299-306		
		SASLHLPK	23	307-314		
		LSITGTLDK	24	315-324		
		SVLGQLGITK	25	325-334		
		VFSNGADLSGVTEEAPLK	26	335-352		
		AVLTIDEK	27	360-367		
4704	353	TDTSHHDQDHPFNK	13	35-49		
		FLEDFK	15	154-160		
		KQINDYVEK	16	179-187		
		QINDYVEK	17	180-187		
		DTEEDFHVDQATTVK (M1A allele)	18	226-241		
		DTEEDFHVDQVTTVK (M1V allele)	19	226-241		
		LSSWVLLMK + 1 Oxidation (M)	28	259-267		
		FLENEDR	21	299-305		
		FLENEDRR	22	299-306		
		SASLHLPK	23	307-314		
		LSITGTLDK	24	315-324		
		SVLGQLGITK	25	325-334		
		VFSNGADLSGVTEEAPLK	26	335-352		

**Table 5.** Identification of the protein spots that were altered between the studied groups.

Spot exp1	Spot exp2	Peptide	Seq ID No.	aa	Identification in database	ID number database
		AVLTIDEK	27	360-367		
		LGMFNIQHCK (Cys-CAM)	29	248-257		
4705	355	QINDYVEK	17	180-187	Alpha-1-antitrypsin	P01009
7206		LSITGTYDLK	24	315-324	Alpha-1-antitrypsin	P01009
		SVLGQLGITK	25	325-334		
		VFSNGADLSGVTEEAPLK	26	335-352		
4801RBH		LLELTGPK	30	86-93	Alpha-1B-glycoprotein	P04217
4803	375	ATWSGAVLAGR	31	386-396	Alpha-1B-glycoprotein	P04217
		FALVREDR	32	313-320		
1RBH		CLAPLEGAR (cys-CAM + ox)	33	304-312	Alpha-1B-glycoprotein	P04217
		FALVREDR	32	313-320		
901RBH		LETPDFQLFK	34	32-41	Alpha-1B-glycoprotein	P04217
		ATWSGAVLAGR	31	386-396		
		LLELTGPK	30	86-93		
		EVPLNTIIFMGR + 1 Oxidation (M)	35	446-457		
5702		DYVSQFEGSALGK	36	52-64	Antithrombin-III	P01008
6102	149	VQPYLDDDFQK	37	121-130	Apolipoprotein A-I	P02647
		[916.56] <sup>+</sup> ALKED[360.25] <sup>+</sup> (aa 208 : N → D)	38	201-212		
		ATEHLSTLSEK	39	220-230		
		AKPALEDLR	40	231-239		
		LSPLGEEMR + 1 Oxidation (M)	41	165-173		
		THLAPYSDELK	42	185-195		
		LLDNWDSVTFSK	43	70-83		
		DSGRDYVSQFEGSALGK	44	48-64		
		LEALKENGGR	45	202-212		
		QGILLPVLESFK	46	240-250		
		VEPLRAELQEGAR	47	143-155		
6303	146	DYVSQFEGSALGK	36	52-64	Apolipoprotein A-I	P02647

**Table 5.** Identification of the protein spots that were altered between the studied groups.

Spot exp1	Spot exp2	Peptide	Seq ID No.	aa	Identification in database	ID number database
7101	285	VQPYLDDFQK	37	121-130	Apolipoprotein A-I	P02647
		[916.56] <sup>+</sup> ALKED[360.27] <sup>+</sup> (aa208 : N → D)	38	201-212		
		ATEHLSTLSEK	39	220-230		
		LSPLGEEMRDR + 1 Oxidation (M)	48	165-175		
		LSPLGEEMR + 1 Oxidation (M)	41	165-173		
		THLAPYSDELK	42	185-195		
		DSGRDYVSQFEGSALGK	44	48-64		
		DYVSQFEGSALGK	36	52-64		
		[1315.83] <sup>+</sup> DNDDSVTSTFSK (aa 74: W→D)	49	70-83		
		QEMSKDLEEVK + 1 Oxidation (M)	50	108-118		
		VQPYLDDFQK	37	121-130		
		VQPYLDDFQKK	51	121-131		
		LSPLGEEMR + 1 Oxidation (M)	41	165-173		
		LSPLGEEMRDR + 1 Oxidation (M)	48	165-175		
		THLAPYSDELK	42	185-195		
		LEALKED[360.25] <sup>+</sup> (aa 208 : N → D)	52	202-212		
		LEALKENGAR	45	202-212		
		ATEHLSTLSEK	39	220-230		
		AKPALEDLR	40	231-239		
		DLATVYVDVLK	53	237-247		
		QGLLPVLESFK	46	240-250		
		QKLHELQEK (E → pyroglutamic acid)	54	156-164		
		VEPLRAELQEGAR	47	143-155		
		LLDNWDSVTSTFSK	43	70-83		
		DEPPQSPWDR + 1 Oxidation (W)	55	25-34		
		DLATVYVDVLK	53	37-47		
		VSFLSALLEEYTK	56	251-262		
		KWQEEMELYR + 1 Oxidation (M)	57	131-140		

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Spot exp1	Spot exp2	Peptide	Seq ID No.	aa	Identification in database	ID number database
4310	144	THLAPYSDELK	42	185-195	Apolipoprotein A-I	P02647
	143	THLAPYSDELK	42	185-195	Apolipoprotein A-I	P02647
4606+4605		LGEVNTYAGDLQK	58	66-78	Apolipoprotein A-IV	P06727
		LLPHANEVSQK	59	113-123		
		QLTPYAQR	60	156-163		
		IDQNVVELKGR	61	190-200		
		LTPYADEFK	62	201-209		
		ISASAEELK	63	256-264		
		LAPLAEDVR	64	267-275		
		ALVQQMEQLR + 1 Oxidation (M)	65	317-326		
5402	81	LEPYADQLR	66	135-143	Apolipoprotein A-IV	P06727
		IDQNVVELKGR	61	190-200		
		LTPYADEFK	62	201-209		
		IDQTVVELR	67	212-220		
		ISASAEELK	63	257-264		
		LAPLAEDVR	64	267-275		
		ALVQQMEQLR + 1 Oxidation (M)	65	317-326		
		RVEPYGENFNK	68	306-317		
		SLAPYAQDTQEK	69	222-233		
		LGEVNTYAGDLQK	58	66-78		
6502		KVEQAVETEPEPELR	4	19-33	Apolipoprotein E	P02649
		AYKSELEEQLTPVAEETR	11	91-109		
		LSKELQAAQAR	12	111-121		
		AATVGSLAGQPLQER	7	210-224		
		AKLEEQAQQIR	2	259-269		
		LQAEAFQAR	1	270-278		
5502	110	LQAEAFQAR	1	270-278	Apolipoprotein E	P02649
		AKLEEQAQQIR	2	259-269		

**Table 5.** Identification of the protein spots that were altered between the studied groups.

Spot exp1	Spot exp2	Peptide	Seq ID No.	aa	Identification in database	ID number database
		LLRDADDLQK	3	166-175		
		KVEQAVETEPEPELR	4	19-33		
	114	LQAEAFQAR	1	270-278	Apolipoprotein E	P02649
		AKLEEQAQQIR	2	259-269		
		LGPLVEQGR	5	199-207		
		VQAAVGTSAAPVPSDNH	6	301-317		
	272	LGPLVEQGR	5	199-207	Apolipoprotein E	P02649
	862	LGPLVEQGR	5	199-207	Apolipoprotein E	P02649
	681	KVEQAVETEPEPELR	4	19-33	Apolipoprotein E	P02649
	480	LQAEAFQAR	1	270-278	Apolipoprotein E	P02649
		LGPLVEQGR	5	199-207		
		AKLEEQAQQIR	2	259-269		
		ALMDETMKELK + 2 Oxidations (M)	70	80-90		
3405		ELDESLQVAER	71	326-336	Apolipoprotein J	P10909
3505		ELDESLQVAER	71	326-336	Apolipoprotein J	P10909
4401	323	ELDESLQVAER	71	326-336	Apolipoprotein J	P10909
		KYNELK	72	340-346		
		FMETVAEK + 1 Oxidation (M)	73	430-437		
5302	108	ELDESLQVAER	71	326-336	Apolipoprotein J	P10909
		EILSVDCSTNNPSQAK + 1 (cys-CAM)	74	307-322		
8601		TLLSNLEEK	75	69-78	Apolipoprotein J	P10909
		IDSLLNDR	76	159-167		
		ASSIIDELFQDR	77	183-194		
5202		AGALNSNDAFVLK	78	585-597	Gelsolin	P06396
		YIETDPANR	79	730-738		
6404		AGALNSNDAFVLK	78	585-597	Gelsolin	P06396
		TGAQELLR	80	616-623		
5004	411	TEGDGVYTLNDKK	81	60-72	Haptoglobin-1/2	P00737



**Table 5.** Identification of the protein spots that were altered between the studied groups.

Spot exp1	Spot exp2	Peptide	Seq ID No.	aa	Identification in database	ID number database
		TEGDGVYTLNDKKQWINK + 1 ox (W)	82	119-131		P00738
				60-77		P00737
5903RBH		NFPSPVDAAFR	83	119-136		P00738
		GGYTLVSGYPK	84	92-102	Hemopexin	P02790
8902RBH		NFPSPVDAAFR	83	333-343		
		QGHNSVFLIK	85	92-102	Hemopexin	P02790
		DYFMPCPGR + 1 (cys-CAM + ox) + 1 ox (M)	86	103-112		
				226-234		
4701RBH		GGYTLVSGYPK	84	333-343		
		SAVQGPPER	87	169-177	Ig alpha-1 chain C region (heavy)	P01876
4804		QEPSQGTTTFAVTSILR	88	283-299		
		TPLTATLSK	89	213-221	Ig alpha-1 chain C region (heavy)	P01876
4702		TVGSDTFYSFK	90	65-75	Kininogen	P01042
		QVVAGLNFR	91	188-196		
		YFIDFVAR	92	317-324		
8101		APEAQVSVQPNFQQDK	93	23-38	Prostaglandin-H2 D- isomerase	P41222
9209		TMLLQPAGSLGSYSYR + 1 Oxidation (M)	94	93-108		
		AQGFTEDTIVFLPQTDK	95	169-185		
		[1617.85] <sup>+</sup> EAQVSVQPNF[518.26] <sup>+</sup>	96	23-38	Prostaglandin-H2 D- isomerase	P41222
6001		TMLLQPAGSLGSYSYR + 1 Oxidation (M)	94	93-108		
7102		AADDTEPFASGK (aa 61 : W → D)	97	56-68	Transthyretin	P02766
		[603.41]PLMVK	98	21-35	Transthyretin	P02766
7108	274	GPTGTGESKCPLMVK (Cys(O <sub>3</sub> H))	99	21-35	Transthyretin	P02766

**Table 5.** Identification of the protein spots that were altered between the studied groups.

Spot exp1	Spot exp2	Peptide	Seq ID No.	aa	Identification in database	ID number database
3601RBH		GPTGTGESKCPLMVK (Cys(O <sub>3</sub> H)/ M : oxidation to sulphone)	99	21-35	Vitamin D-binding protein	P02774
		AADDTWEPFASGK (W + 2*16 Da)	100	56-68		
		AADDTDEPFASGK (aa 61 : W → D)	97	56-68		
		AADDTWEPFASGK	100	56-68		
		KAADDTWEPFASGK	102	55-68		
		TSESGELHGLTTEEFVEGIYK	103	69-90		
		HLSLLTTLNR	104	208-218		
		YTFELSR	105	346-352		
		THLPEVFLSK	106	354-363		
		VLEPTLK	107	364-370		
4411		ELSSFIDK	108	395-402	Vitamin D-binding protein	P02774
		VCSQYAAAYGEK (cys-CAM + ox)	109	219-229		
		VMDKYTFELSR + 1 Oxidation (M)	110	342-352		
		YTFELSR	105	346-352		
		THLPEVFLSK	106	354-363		
		VLEPTLK	107	364-370		
		[1433.61] <sup>+</sup> CCDVEDSTTCFNAK (1 cys-CAM + ox, 2 Dha)	111	371-388		
		ELSSFIDK	108	395-402		
		AKLPDATPK	112	428-436		
		AGEVQEPELR	113	239-248		
2402	88	QDPPSVVVTSHQAPGEK	101	201-217	Zinc-alpha-2-glycoprotein	P25311